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DB=USPT; PLUR=YES; OP=OR

<u>L27</u>	L1 and fabric	0	<u>L27</u>
<u>L26</u>	L1 and fiber	0	<u>L26</u>
<u>L25</u>	l1 and ozokerities	0	<u>L25</u>
<u>L24</u>	l1 and woven	0	<u>L24</u>
<u>L23</u>	l1 and non-woven	0	<u>L23</u>
<u>L22</u>	l21 and 424/\$.ccls.	5	<u>L22</u>
<u>L21</u>	L20 and patch	25	<u>L21</u>
<u>L20</u>	((release adj liner) same (release adj paper))	189	<u>L20</u>
<u>L19</u>	l18 and paper	51	<u>L19</u>
<u>L18</u>	l17 and patch	61	<u>L18</u>
<u>L17</u>	(peeling same (release adj liner))	271	<u>L17</u>

DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; PLUR=YES; OP=OR

<u>L16</u>	(release adj liner) same (peeling adj paper)	0	<u>L16</u>
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DB=USPT; PLUR=YES; OP=OR

<u>L15</u>	(release adj liner) and (peeling adj paper)	5	<u>L15</u>
<u>L14</u>	adhesive and l1	1	<u>L14</u>
<u>L13</u>	l1 and peel	0	<u>L13</u>
<u>L12</u>	redetachable adj protective adj layer	1	<u>L12</u>
<u>L11</u>	L1 and (release adj liner)	0	<u>L11</u>
<u>L10</u>	l1 and redetachable	0	<u>L10</u>
<u>L9</u>	l1 and detachable	0	<u>L9</u>
<u>L8</u>	L5 and (barrier adj layer)	57	<u>L8</u>
<u>L7</u>	d l6 1-5L6	1867880	<u>L7</u>
<u>L6</u>	L5 and (barrier adj layer)	57	<u>L6</u>
<u>L5</u>	L4 and patch	1054	<u>L5</u>
<u>L4</u>	release adj liner	5820	<u>L4</u>
<u>L3</u>	L1 and (liner)	0	<u>L3</u>
<u>L2</u>	L1 and (release or liner)	1	<u>L2</u>
<u>L1</u>	5071704.pn.	1	<u>L1</u>

END OF SEARCH HISTORY

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L22: Entry 2 of 5

File: USPT

Jun 29, 1999

DOCUMENT-IDENTIFIER: US 5916587 A

TITLE: Transdermal delivery matrix for piroxicam

Brief Summary Text (7):

Francoeur et al., U. S. patent application Ser. No. 925,641(Oct. 31, 1986), disclose topical compositions of amlodipine, doxazosin, glipizide, piroxicam and other drugs containing aqueous solution of ethanol, 1-alkylazacycloheptane-2-one and oleic acid. However, this method is impossible to make a thin patch and is only possible to make gel, ointment and liquid compositions.

Brief Summary Text (8):

In Japanese, Laid-Open Patent Ser. No. 91-251534, there is disclosed patch compositions for increased dermal penetration of piroxicam by adding penetration enhancer, selected from polyoxyethylenealkyl ethers or alkanolamides, and dissolving assistant agent of polyvinylpyrrolidone to pressure-sensitive adhesives of copolymer of vinylpyrrolidone and methacrylic ester. However, this composition is also inferior in percutaneous absorption because polyvinylpyrrolidone of dissolving agent acts only a dissolving assistant role and does not assist the absorption of drug.

Brief Summary Text (9):

For the reasons mentioned above, as result of concentrative researches about the improvement of percutaneous absorption and high content of drug in patch, the present inventors found that, in case of using certain absorption assistants, the excessively dissolved piroxicam is included in matrix and simultaneously the percutaneous absorbability is surprisingly enhanced, so that have been perfected the present invention.

Detailed Description Text (10):

The preparation of the transdermal delivery system according to the present invention is accomplished as follows. The active substance is dissolved in the solvent and enhancer to form a solution or a suspension. This solution or suspension is added to the polymer and mixed for about 20.about.30 minutes and then allowed to stand for about 20.about.60 minutes to eliminate the air bubbles. This mixture is cast on the impermeable membrane, a polyethylene film or aluminized polyethylene film made by 3M Company (e.g. 3M-Scotchkpak 1006 or 3M 1012) and dried at about 40.degree. C. to 50.degree. C. for about 30.about.60 minutes. After drying the coated matrix, a release liner, such as a silicon release paper, or the like which are well known, is placed over the exposed surface of the matrix. Then the system is die-cut into a optimum size. If multiple matrix layers are required, each subsequent layer is cast over or overlaps on the previous layer. The finished system is put into a pouch and hermetically sealed.

Detailed Description Text (44):

Male rats of Wister strain, weighing 287.+- .11 g (7.about.9 weeks old), were depilated and allowed to stand overnight for use in the experiment (Topical applied:5 mg/kg, systemical applied:30 mg/kg). Then, 0.1 ml of 1% carrageenin solution was hypodermally injected into left hind leg after 3 hours of applying patch. The swelling inhibition ratio is measured by plethysmometer (UGO BASILE TYPE 7150) at intervals of 1 hour for a 6 hours period after injection. The results are presented in FIG. 3.

Detailed Description Text (47):

In the present invention, in vitro test, human cadaver skin was obtained from Ohio Valley Tissue And Skin Center and hydrated for 24 hours with phosphate buffer (pH6.0 Standard buffer solution in U.S. Pharmacopoeia) before experiments. The hydrated skin was mounted in Frantz cell. The upper side of skin, having an available diffusion area of 1.0 cm.sup.2, was exposed to ambient conditions. The lower side was filled by the receptor medium (5.0 ml, pH 6.0 Standard buffer solution in U.S. Pharmacopoeia) being stirred and kept at 32.degree. C. Piroxicam patch directed in the present invention was adhered to upper side of skin and fixed with clamp. For 72 hours samples were withdrawn and replaced by fresh receptor medium keeping an infinite sink. The flux of piroxicam penetrating the skin was determined by measuring the concentration by HPLC system.

Detailed Description Text (48):

In vivo test, fifty male volunteers were subjected to residual test of patch.

Detailed Description Text (49):

Piroxicam patches, directed in the present invention, of which content was known were adhered to the outer side of volunteer's upper arm and maintained there for 72 hours, and then removed. The absorbed amount of piroxicam was determined by measuring the residual amount of piroxicam in removed patch by HPLC system.

Detailed Description Text (54):

Fifty patients (30 male/20 female) were subjected to the systemical remedial effect test on patch in the present invention. The adhesion site of patch was same as that in Experiment 2. The results are presented in Table 2.

Detailed Description Text (56):

Thirty male people were subjected to skin irritation test on effect of the existence of corticosteroid in piroxicam patch.

Detailed Description Text (57):

The patch was applied to te back of volunteers for 48 hours and the skin was evaluated for evidence of erythema, edema or more severe skin changes occurring 24, 48 and 72 hours after removal of patch. The results are presented in Table 3.

Detailed Description Paragraph Table (3):

TABLE 2		The Remedial Effect of Piroxicam Patch. Effect Responsibility (%) (male/female)									
		Age -2		-1		0		+1		+2	
45/60	19/0	41-50	--	50/20	50/80	--	51-60	--	33/0	67/100	--
									61-	--	25/50
									25/50	25/25	
50/25	--	Partial	0	3.3/10	40/25	50/65	6.7/0	Average(M/F)	Total	Average	0
50.0	4.0										40.0
*Annotations -2: more worse of symptoms, -1: no change of symptoms 0: better of symptoms, +1: very better of symptoms +2: absent of symptoms											

Detailed Description Paragraph Table (4):

TABLE 3		Results of Skin Irritation Time (hr)							
Samples	24 48 72	Patch of Example 13 0 0 0							
Patch of Example 13	2 1 0	without hydrocortisone Patch of Example 14 0 0 0 Patch of Example 14							
1 1 0		without hydrocortisone							
No extraordinary reaction	1:	Slight erythma 2: Erythma or slight edema							

Current US Original Classification (1):

424/448

Current US Cross Reference Classification (1):

424/449

First Hit Fwd Refs**End of Result Set**

L22: Entry 5 of 5

File: USPT

Mar 6, 1990

DOCUMENT-IDENTIFIER: US 4906475 A
TITLE: Estradiol transdermal delivery system

Detailed Description Text (9):

The preparation of the transdermal delivery system according to the present invention is accomplished as follows. The active substance is dissolved in the solvent and enhancer to form a solution. The solution is added to the polymer and mixed for about 20-30 minutes and then allowed to stand for about 20-60 minutes to eliminate the air bubbles. This mixture is cast on the impermeable membrane, a polyethylene film or aluminized polyethylene film made by 3M Company (e.g. 3M-Scotchpak 1006 or 3M-1012) and dried at about 40.degree. C. to 50.degree. C., for about 20-40 minutes. After drying the coating, a release liner 16, such as a silicon release paper or the like which are well known, is placed over the exposed surface of the matrix. Then the system is die cut into a optimum size. If multiple matrix layers are required, each subsequent layer is cast over or overlaps the previous layer. The finished system is put into a pouch and hermetically sealed.

Current US Original Classification (1):
424/449

Current US Cross Reference Classification (1):
424/447

Current US Cross Reference Classification (2):
424/448

Other Reference Publication (8):

Acharya, et al., "Observations on 17-B-Hydroxysteroid Dehydrogenase in the Brood Patch of House Sparrow", Current Sci., vol. 53, No, 3, pp. 160-162, 2/1984.

Other Reference Publication (10):

Jones, et al., "Incubation Patch of the Chicken", Gen. and Comp Endocr. vol. 15, pp. 398-403, 1970.

Other Reference Publication (11):

Hutchinson, et al., "The Effects of Estrogen Progesterone and Prolactin on Brood Patch Formation in Ovariectomized Canaries", J. Endocr., vol. 39, pp. 379-385 (1967).

Drawing Description Text (4):

FIG. 3 is an illustration of a controlled release device which has an adhesive layer, an impermeable backing layer, a reservoir layer, and a diffusion rate limiting membrane.

Detailed Description Text (13):

For controlled release devices in which the reservoir layer 12 does not provide the necessary "tacky" surface for adhering to the impermeable backing layer 16 and the diffusion rate limiting layer 14, it is desirable to provide a clip or other component for securing the layers of the device together. This component may be a miniature clip, such as the clip shown in phantom at 18 in FIG. 1 which is secured over each face of the device, or a small amount of an adhesive, such as an epoxy, applied to the edges. Alternatively, the laminate layer edges may be secured by heat or solvent sealing techniques. In addition to providing a support system for the layers of the device, the clip 18 or other components prevent the loss of the active component from the edges of the reservoir.

Detailed Description Text (21):

FIG. 3 depicts another embodiment of the present invention, generally designated laminate 30. This preferred embodiment is suitable for adhering to a surface while emitting vapors, liquids, or dissolved solids of choice. In accordance with the teachings of the present invention the features of this embodiment include a diffusion rate limiting membrane 34, a reservoir layer 32, adjacent the diffusion rate limiting membrane layer, a vapor and liquid impermeable backing layer 36 adjacent the diffusion rate limiting membrane layer, and a pressure sensitive contact adhesive layer 38 adjacent the impermeable backing layer.

Detailed Description Text (23):

Adjacent the diffusion rate limiting membrane layer 34 is the reservoir layer 32 incorporating the active compound of choice. Reservoir layer 32 may consist of any of the polymeric forms discussed above in the description of FIG. 1. Adjacent the reservoir layer 32 is a vapor and liquid impermeable backing 36. In addition to being a barrier to the active compound, the impermeable backing layer 36 further provides a means to prevent the active compound from interfering with the function of the adhesive as will be discussed below.

Detailed Description Text (24):

Adjacent the vapor and liquid impermeable backing 36 is an adhesive layer 38. The adhesive may be any pressure sensitive contact adhesive suitable for applying to a surface such as the acrylate contact adhesives. When the controlled release device is intended to be used on the skin or any tissue area of a person the contact adhesive must additionally be non-toxic, biocompatible, and hypoallergenic. In particular the biocompatible adhesive may be suitable acrylates, and hydroxypropyl cellulose, medical grade silicone adhesives and their derivatives.

Detailed Description Text (25):

The adhesive is applied to the impermeable backing layer 36 of the laminate. The backing material prevents the diffusing active compound from diffusing into the adhesive layer 38 and diminishing the effectiveness of the adhesive by solubilizing it or destroying the surface-adhesive bond. It is also undesirable for the active compound to diffuse in the direction of the adhesive since the target release point is the environment bound by the diffusion rate limiting membrane 34.

Detailed Description Text (26):

The attendant advantages of the embodiment of the present invention as illustrated in FIG. 3 is the ability of the controlled release device to be conveniently adhered to any surface which will accept the pressure sensitive contact adhesive layer. For example, it is contemplated within the scope of the invention to form a laminate as depicted in FIG. 3 with a reservoir layer 32 which incorporates an air

freshener emitting compound and having dimensions of from about 5 cm.sup.2 to about 500 cm.sup.2 and about 0.2 mm thick. The device may be adhered to the surface of the interior of an automobile or and the wall surface of an interior room. It will effectively release the air freshener over a desired time period at a substantially constant rate.

Detailed Description Text (29):

A variation of the embodiment of the present invention illustrated in FIG. 3 is detailed in the laminate of FIG. 4. In accordance with FIG. 4 a decorative layer 50 is adjacent the diffusion rate limiting membrane layer 44. A reservoir layer 42 is adjacent both the diffusion rate limiting, membrane layer 44, and an impermeable backing layer 46. An adhesive layer 48 is adjacent the impermeable backing layer 46. The diffusion rate limiting membrane 44, reservoir layer 42, impermeable backing layer 46, and adhesive layer 48 have properties and characteristics as described for FIG. 3. The decorative layer 50 preferably is comprised of a thin highly porous material of polyester base which freely allows the released vapors to diffuse from one surface to the other surface and into the surrounding environment.

Detailed Description Text (33):

A perfume emitting device comprising the general laminate form shown in FIG. 4 is prepared using the following procedure and materials. An adhesive solution of a medical grade silicone adhesive was prepared by dissolving the silicone adhesive in isopropyl alcohol to a 5% by weight adhesive content. A peeling layer consisting of a standard form release paper was spread in a flat cast vehicle. The 5% solution of adhesive in isopropyl alcohol was then poured onto the peeling layer of standard release paper and the isopropyl alcohol was subsequently allowed to evaporate. The resulting adhesive layer was between 50 to 75 um thick.

Detailed Description Text (34):

After the isopropyl alcohol was evaporated, a gas and liquid impermeable membrane layer consisting of an approximately 50 um membrane of a medium low density polyethylene/aluminized polyester/ethylene vinyl acetate was placed on the adhesive layer. A polymer gel of perfume emitting compound and hydroxypropyl cellulose was then prepared by adding enough of a perfume to powdered hydroxypropyl cellulose to prepare a 50% by weight perfume-polymer gel. The hydroxypropyl cellulose is KLUCEL with a molecular weight of 1,000,000.

Detailed Description Text (39):

An insect repellent emitting device comprising the general laminate form shown in FIG. 4 is prepared using the following procedure and materials. An adhesive solution of medical grade silicone adhesive layered on a peeling layer is prepared according to the method described in the first paragraph of Example 1.

Detailed Description Text (40):

A gas and liquid impermeable membrane layer consisting of an approximately 50 micron thick membrane layer of a medium low density polyethylene/aluminized polyester/ethylene vinyl acetate is placed on the adhesive layer. A polymer gel of insect repellent emitting compound and hydroxypropyl cellulose is then prepared by adding enough of an insect repellent to powdered hydroxypropyl cellulose to prepare a 50% by weight insect repellent-polymer gel. The hydroxypropyl cellulose is KLUCEL with a molecular weight of 1,000,000.

Detailed Description Text (45):

A breath freshener comprising the general laminate shown in FIG. 3 is prepared using the following procedure and materials. An adhesive consisting of a polysaccharide type mucoadhesive is spread on a peeling layer of standard form release paper to a thickness of about 100 um. A liquid impermeable membrane layer consisting of an approximate 100 um membrane of aluminized polyethylene terephthalate is placed on the adhesive layer.

Detailed Description Text (48):

A device useful for the sustained and controlled release of air fresheners comprising the general laminate form shown in FIG. 4 is prepared using the following procedure and materials. An acrylate adhesive is spread on a peeling layer of standard form release paper to a thickness of approximately 75 um. A gas and liquid impermeable membrane layer consisting of an approximately 200 um membrane of a medium low density polyethylene/aluminized polyester/ethylene vinyl acetate is placed on the adhesive layer. An air freshener is incorporated in a 400 um thick layer of ACCUREL porous polypropylene having a 80% void volume by immersing the ACCUREL in the air freshener for three hours. Following the immersion step the ACCUREL is placed on the impermeable membrane layer which is followed by placing a diffusion rate limiting membrane of cellulose nitrate having a pore size of about 0.1 microns. The device is finished with a decorative covering of polyester which provides an added ornamental appeal.

CLAIMS:

1. A device useful for the controlled release of a perfume or fragrance, said device forming a laminate comprising:

a decorative layer consisting of an artistic design formed on a 50 um polyester film;

a diffusion rate limiting membrane layer adjacent said decorative layer, said diffusion rate limiting membrane consisting of a 40 um thick ethylene vinyl-acetate film;

a reservoir layer adjacent said diffusion rate limiting membrane layer, said reservoir layer comprising a gelled mixture of perfume and hydroxypropyl cellulose;

a vapor and liquid impermeable backing layer adjacent said reservoir layer, said impermeable backing layer consisting of a 50 um thick medium density polyethylene/aluminized polyester/ethylene vinylacetate;

a pressure sensitive contact adhesive layer adjacent said vapor and liquid impermeable backing layer, said adhesive layer consisting of a medical grade silicone adhesive.

2. The device of claim 1 further comprising one or more clips extending from adjacent said decorative layer to adjacent said adhesive layer.

First Hit Fwd Refs**End of Result Set**

L14: Entry 1 of 1

File: USPT

Dec 10, 1991

DOCUMENT-IDENTIFIER: US 5071704 A

TITLE: Device for controlled release of vapors and scents

Abstract Text (1):

A controlled release device useful for the release of vapors or liquids is described. The device is a multilayered laminate consisting of a reservoir layer which incorporates an active compound, such as a perfume or fragrance or insect repellent, an impermeable membrane layer adjacent the reservoir layer and a diffusion rate limiting membrane layer adjacent the reservoir layer. The device preferably includes an adhesive layer for adhering the device to skin or a surface and an ornamental decorative layer.

Brief Summary Text (8):

U.S. Pat. No. 4,880,690 describes a perfume patch which is a laminate of polyurethane in combination with other layers including an impermeable backing and adhesive layer. The patch incorporates a perfume in the polyurethane layer and is intended to be adhered to the user's skin in areas such as behind the ear. Additionally, the patch may have an added pigment or decorative design on the polyurethane layer which lends some artistic appeal to the laminate.

Brief Summary Text (11):

Controlled release devices are used extensively in the pharmaceutical industry to provide therapeutic and diagnostic compounds to patients over periods of time ranging from minutes to days. In particular, skin patches have been used successfully in administering medications transdermally for several hours at a time with just one patch application. In particular, a patch described in U.S. Pat. No. 4,031,894 for delivering the sea sickness medication, scopolamine, is a five layer laminate designed to be attached to the skin behind the user's ear and deliver the drug through the patch's adhesive layer and into the user's circulatory system.

Brief Summary Text (19):

The present invention accomplishes the above described objectives by providing a controlled release device in the form of a laminate which consists of at least one layer of a diffusion rate limiting membrane placed adjacent a second layer which incorporates the active compound. The controlled release devices of the present invention may be decoratively embellished with ornamental designs without interfering with the release properties. Additionally, the laminate design provides a means of maintaining an adhesive layer which allows the device to adhere to a variety of surfaces for the duration of its active life. The controlled release device of the present invention may be configured in any of a variety of shapes and sizes depending upon the active compound of choice, the environment of its intended use, and the duration of its intended use.

Brief Summary Text (21):

In accordance with the present invention, the controlled release device may be configured with an impermeable backing and an adhesive layer which allows the device to adhere to wall surfaces, skin, clothing, mucosa tissue, and other items without affecting the release properties. Additionally, the adhesive-surface bond remains intact during its period of use without interference from the active compound.

First Hit Fwd Refs

L6: Entry 1 of 57

File: USPT

Jun 29, 2004

DOCUMENT-IDENTIFIER: US 6756052 B1

TITLE: Device and method for increasing the transdermal permeation of medicaments

Brief Summary Text (2):

The transdermal administration of pharmaceutical active substances has been known from the time of the first commercial use of a scopolamine transdermal therapeutic system (Scopoderm TTS). Other active substances (nitroglycerine, estradiol, clonidine, isosorbide dinitrate, fentanyl, nicotine, norethisterone etc.) as well are now offered in the form of such a TTS. These active substance patches are adhered to the skin of a patient. The active substance is then released in a controlled manner from the TTS to the skin of the patient, travels through the various layers of the skin, and, finally, enters the circulation.

Brief Summary Text (10):

This object is achieved by a device which comprises a component which brings about a local temperature increase in the skin and/or increases the circulation. The device of the invention can be, for example, an ointment, a solution, a suspension, an emulsion, a foam, a paste, a gel or a patch, a patch of this kind being a preferred embodiment.

Brief Summary Text (26):

Owing to the difficulty in controlling the amount applied in this case of the component which brings about a local temperature increase of the skin, and owing to any concomitant adhesion problems of the TTS on the skin, the preferred embodiment is, as stated, a patch.

Brief Summary Text (27):

A patch of this kind, i.e., a dermal or transdermal therapeutic system, can comprise the following structural elements: an active substance impermeable backing layer, an active substance reservoir, an active substance release controlling (semipermeable or microporous) membrane, an adhesive layer containing active substance, and a redetachable protective layer (known as the release liner).

Brief Summary Text (29):

The simplest embodiment of this case is a pressure sensitive adhesive layer which comprises the component that brings about a local temperature increase and/or increase in circulation in the skin and which is equipped with a backing layer impermeable to said component. In this embodiment, the device consists of two separate devices, namely an active substance release device and the device containing the component which brings about a local temperature increase and/or circulation increase in the skin. The active substance release device, an active substance TTS for example, is applied first of all to the skin of the patient. Then the device containing the component which brings about a local temperature increase of the skin is placed atop it and judiciously fixed--for example, by means of a pressure sensitive adhesive layer located on the bottom, pressure sensitive adhesive strips located on the edge of the device, or a further, cover patch. Likewise preferred is an embodiment in which an outer segment containing the component which brings about a local temperature increase and/or circulation increase in the skin is disposed around an inner segment which contains the active substance intended for transdermal administration. The form of the inner segment is in principle not critical; it can be circular, rectangular or square. The form of

the outer segment is likewise in principle not critical; it can also be circular, rectangular or square. Alternatively, the outer segment can be disposed around the inner segment in the form of a ring or as two or more sections which are, for example, rectangular or semicircular. This embodiment is particularly suitable since it profits from the formation of a horizontal concentration gradient in the epidermis and in the dermis/subcutis. Although this so-called lateral diffusion can be derived from the structure of the stratum corneum with its lamellar lipid-water bilayers, this phenomenon has, surprisingly, to date not been considered by those skilled in the art for a practical implementation in terms of increasing the rate of penetration into the skin and/or of travel through the skin, in particular for increasing the transdermal absorption rate of an active substance applied to the skin.

Brief Summary Text (32):

A preferred embodiment of this kind can likewise be produced by processes known to the skilled worker, as described, for example, in DE 37 14 140, DE 38 09 978 and DE 41 10 027. In order to avoid repetition, the relevant section of the disclosure contents of these documents has not been reproduced here but is considered to be incorporated by reference. It is clear that when producing the outer segment the component which brings about a local temperature increase of the skin must be incorporated into the matrix forming the outer segment, in the appropriate working step. The spatial separation of the segments containing the component which brings about a local temperature increase and/or circulation increase in the skin from the segments containing the active substance intended for transdermal administration is achieved by horizontal or vertical barrier layers or material voids.

Detailed Description Text (3):

Three samples of a commercially available estradiol active substance patch (Vivelle.RTM.) were each applied centrally to circular specimens of complete human skin, measuring 4.52 cm.sup.2 . The skin samples thus prepared were placed for 72 h in modified Franz cells, there being no acceptor medium, so as to avoid artefacts as a result of back-diffusion into the cells. After the end of this time, the active substance patches were removed and the skin below the application site was punched out exactly. Further circular segments were punched out from the skin sample, each situated further and further from the core segment, that is, the actual release area of the TTS.

Detailed Description Text (6):

An in vivo animal experiment was performed on two groups of rats each containing n=6 animals. Each of the animals from both groups had adhered to it a TTS containing a poorly absorbable active substance (morphine base). In the animals of the first experimental group, a cover patch containing an effective amount of a component which brings about a local temperature increase of the skin (ABC patches from Beiersdorf, Hamburg (DE)) was applied over the actual active substance release TTS. The effective substances of said cover patch are capsaicin and arnica extract. The areal skin contact of the cover patch in comparison to that of the active substance release TTS was 3 to 1.

Detailed Description Text (7):

The animals of the second experimental group (the control group) received as cover patch a self-adhesive occlusive film without a component which brings about a local temperature increase of the skin (Opraflex from Lohmann, Neuwied (DE)). The areal skin contact of the cover patch in comparison to that of the active substance release TTS was likewise 3 to 1.

Detailed Description Text (8):

After the end of the 24-hour period of wear, the patch dressings were removed and were assayed for residues of morphine base. The results are summarized in Table 2 and show that the use of a cover patch containing an effective amount of a component which brings about a local temperature increase of the skin increased the

transdermal absorption rate from 5.7 to 26.4%.

Detailed Description Text (16):

FIG. 2 shows an embodiment in which the component which brings about a local temperature increase and/or circulation increase in the skin is spatially separated by a vertical barrier layer from the reservoir and from the pressure sensitive adhesive layer containing the active substance intended for transdermal administration. The reference symbols have the following meanings: 21=active substance impermeable backing layer, 22=reservoir containing the active substance intended for transdermal application but free from the component which brings about a local temperature increase and/or circulation increase in the skin, 23=pressure sensitive adhesive layer containing the active substance intended for transdermal administration but free from the component which brings about a local temperature increase and/or circulation increase in the skin, 24=pressure sensitive adhesive layer containing the component which brings about a local temperature increase and/or circulation increase in the skin, 25=vertical barrier layer.

Detailed Description Text (17):

FIG. 3 shows an embodiment in which the component which brings about a local temperature increase and/or circulation increase in the skin is spatially separated by a horizontal barrier layer from the reservoir and from the pressure sensitive adhesive layer containing the active substance intended for transdermal administration. The reference symbols have the following meanings: 31=active substance impermeable backing layer, 32=reservoir or pressure sensitive adhesive layer containing the active substance intended for transdermal administration but free from the component which brings about a local temperature increase and/or circulation increase in the skin, 33=pressure sensitive adhesive layer containing the component which brings about a local temperature increase and/or circulation increase in the skin, 34=horizontal barrier layer, 35=skin.

Detailed Description Paragraph Table (2):

	Experimental group with Opraflex cover patch TTS	Initial amount	Residue Released
Verum 1	546.7 .mu.g/cm.sup.2	506.6 .mu.g/cm.sup.2	40.1 .mu.g/cm.sup.2
Verum 2	546.7 .mu.g/cm.sup.2	514.2 .mu.g/cm.sup.2	32.5 .mu.g/cm.sup.2 Verum 3
	546.7 .mu.g/cm.sup.2	538.8 .mu.g/cm.sup.2	7.9 .mu.g/cm.sup.2 Verum 4
	546.7 .mu.g/cm.sup.2	528.0 .mu.g/cm.sup.2	18.7 .mu.g/cm.sup.2 Verum 5
	546.7 .mu.g/cm.sup.2	494.9 .mu.g/cm.sup.2	51.8 .mu.g/cm.sup.2 Verum 6
	546.7 .mu.g/cm.sup.2	510.0 .mu.g/cm.sup.2	36.7 .mu.g/cm.sup.2 Mean:
	515.4 .mu.g/cm.sup.2	31.3 .mu.g/cm.sup.2	

Detailed Description Paragraph Table (3):

	Experimental group with ABC-Warme-Pflaster N cover patch TTS	Initial amount	Residue Released
Verum 1	546.7 .mu.g/cm.sup.2	364.7 .mu.g/cm.sup.2	182.0 .mu.g/cm.sup.2
Verum 2	546.7 .mu.g/cm.sup.2	354.6 .mu.g/cm.sup.2	192.1 .mu.g/cm.sup.2 Verum 3
	546.7 .mu.g/cm.sup.2	442.9 .mu.g/cm.sup.2	103.8 .mu.g/cm.sup.2 Verum 4
	546.7 .mu.g/cm.sup.2	447.9 .mu.g/cm.sup.2	98.8 .mu.g/cm.sup.2 Verum 5
	546.7 .mu.g/cm.sup.2	446.8 .mu.g/cm.sup.2	99.9 .mu.g/cm.sup.2 Verum 6
	546.7 .mu.g/cm.sup.2	359.0 .mu.g/cm.sup.2	187.7 .mu.g/cm.sup.2 Mean:
	402.7 .mu.g/cm.sup.2	144.1 .mu.g/cm.sup.2	

CLAIMS:

4. The device as claimed in claim 1, wherein at least one horizontal barrier layer, at least one vertical barrier layer, at least one gap in the material and/or a mixture of the foregoing is used to-separate spatially the first layer from the second layer.

9. The method according to claim 6, whereas the device comprising said component is selected from the group consisting of an ointment, a solution, a suspension, an emulsion, a foam, a paste, a gel or a patch.

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L13: Entry 3 of 3

File: USPT

Jun 28, 1994

DOCUMENT-IDENTIFIER: US 5324538 A

TITLE: Process for producing composite semipermeable membrane employing a polyfunctional amine solution and high flash point - solvent

Detailed Description Text (2):

The microporous substrate employed in the present invention may preferably have an asymmetric structure along the cross-sectional direction. The microporous substrate may preferably have micropores of which average pore size at the surface of the substrate is 2-500 nm, more preferably 3-30 nm. The microporous substrate may preferably have a thickness of 10-300 .mu.m, still more preferably 30-200 .mu.m. Preferred examples of the material mainly constituting the microporous substrate include polysulfones, polyethersulfones, polyacrylonitriles, cellulose esters, polyphenyleneoxides, polypropylenes, polyvinyl chlorides, polyphenylenesulfidesulfones, polyphenylenesulfones and the like. The microporous substrate may be in the form of a flat membrane or in the form of hollow fiber or tube. The microporous substrate may be reinforced by a woven fabric or a non-woven fabric. Preferred examples of the material constituting the woven fabric or non-woven fabric include polyesters, polypropylenes, polyamides, polyacrylonitriles, regenerated celluloses and acetyl celluloses. In cases where a non-woven fabric is employed, the non-woven fabric may preferably have a weight of 40-200 g/m.². A non-woven fabric having a weight less than this range is not preferred since sufficient reinforcing effect may not be obtained and the polymer solution cast thereon in the production process of the substrate may permeate to the backside.

Detailed Description Text (3):

The microporous membrane may be prepared, for example, by casting 12-25 wt % polysulfone solution in dimethylformamide onto a fabric such as non-woven fabric and immersing the resultant in a coagulation bath. The coagulation bath may preferably contain water or a mixture of water and a solvent. The support on which the polysulfone solution is cast may be immersed in the coagulation bath after evaporating the solvent for a prescribed time. In this case, the time for evaporating the solvent may preferably be 0-60 minutes, more preferably 1-10 minutes. The temperature of the atmosphere in which the evaporation of the solvent is carried out may preferably be 0.degree. C. to the boiling point of the solvent, more preferably 5.degree. C. to (boiling point of the solvent minus 50.degree. C.).

Detailed Description Text (59):

On a polyester non-woven fabric (weight: 120 g/m.²), 20 wt % polyphenylenesulfide sulfone solution in 1,3-dimethyl-2-imidazolidinone was cast to a thickness of about 100 .mu.m and the resultant was immediately immersed in water bath at room temperature so as to gel the polyphenylenesulfide sulfone solution, thereby obtaining a polyphenylenesulfide sulfone microporous substrate. The thus obtained polyphenylenesulfide sulfone microporous substrate was sufficiently washed with water so as to exchange the solvent in the substrate with water.

CLAIMS:

7. The process of claim 1, wherein said microporous substrate is reinforced with a woven-fabric or a non-woven fabric.

First Hit Fwd Refs**End of Result Set**

L13: Entry 3 of 3

File: USPT

Jun 28, 1994

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CLAIMS:

7. The process of claim 1, wherein said microporous substrate is reinforced with a woven-fabric or a non-woven fabric.

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L9: Entry 1 of 1

File: USPT

Dec 10, 1991

DOCUMENT-IDENTIFIER: US 5071704 A

TITLE: Device for controlled release of vapors and scents

Abstract Text (1):

A controlled release device useful for the release of vapors or liquids is described. The device is a multilayered laminate consisting of a reservoir layer which incorporates an active compound, such as a perfume or fragrance or insect repellent, an impermeable membrane layer adjacent the reservoir layer and a diffusion rate limiting membrane layer adjacent the reservoir layer. The device preferably includes an adhesive layer for adhering the device to skin or a surface and an ornamental decorative layer.

Brief Summary Text (19):

The present invention accomplishes the above described objectives by providing a controlled release device in the form of a laminate which consists of at least one layer of a diffusion rate limiting membrane placed adjacent a second layer which incorporates the active compound. The controlled release devices of the present invention may be decoratively embellished with ornamental designs without interfering with the release properties. Additionally, the laminate design provides a means of maintaining an adhesive layer which allows the device to adhere to a variety of surfaces for the duration of its active life. The controlled release device of the present invention may be configured in any of a variety of shapes and sizes depending upon the active compound of choice, the environment of its intended use, and the duration of its intended use.

Brief Summary Text (20):

The controlled release devices of the present invention are multilayer laminates with an active compound incorporated in a reservoir layer. The active compound may be any of a number of useful vapor emitting compounds such as perfumes, various fragrances, air fresheners, insecticides, and insect repellents. Additionally, the active compound may be intended for use in its liquid or dissolved form, e.g. breath fresheners. The laminates of the present invention are constructed such that the active compound diffuses from the reservoir layer into a diffusion rate limiting membrane layer where the vapor or liquid is released into the surrounding environment at a substantially constant rate over the intended life of the device. If desired, for applications in which the controlled delivery device is utilized in visible areas, an ornamental or decorative layer may be incorporated for added appeal.

Drawing Description Text (2):

FIG. 1 is an illustration of a controlled release device which forms a laminate comprising a reservoir and a diffusion rate control membrane, and an impermeable backing.

Drawing Description Text (4):

FIG. 3 is an illustration of a controlled release device which has an adhesive layer, an impermeable backing layer, a reservoir layer, and a diffusion rate limiting membrane.

Detailed Description Text (2):

The present invention is a controlled release device in the form of a laminate which may be utilized in any of a number of applications in which it is desirable to release vapors or liquid from an active compound into the environment surrounding the compound. The controlled release device of the present invention provides a substantially constant controlled rate of release of the vapor or liquid from the device. This is accomplished by incorporating a diffusion rate limiting membrane layer into the laminate which controls the rate at which the active compound diffuses to the surface of the device and vaporizes or dissolves into the environment surrounding the device.

Detailed Description Text (3):

An exemplary controlled release device produced in accordance with the teachings of the present invention is shown in FIG. I. The device 10 as shown is a cross-sectional view of a laminate that consists of three layers: a reservoir layer 12 which incorporates an active compound or compounds, a diffusion rate limiting membrane layer 14 adjacent to the reservoir layer, and an impermeable backing layer 16.

Detailed Description Text (8):

As in the case of all polymers which are suitable for use in the reservoir layer of this invention, both the liquid and the polymer which form the gel must be physically and chemically compatible with the active compound. Any gelled mixtures of oil and polymer and gelled mixtures of water and polymer known in the art and suitably compatible and non toxic may be used. Among these gelled mixtures are oil and polyisobutylene, oil and isoprene, oil and silicone, water and polyvinylpyrrolidone, water and hydroxyethylmethacrylate, and combinations including hydroxypropyl cellulose. In addition to diluents and gelling agents, reservoir 12 may include other materials such as stabilizers.

Detailed Description Text (9):

Referring again to FIG. 1, the diffusion rate limiting membrane layer 14 is a thin membrane of from about 10 microns to about 100 microns. It is a microporous polymer which can be selected from any one of the polymers known in the art which is available as a thin microporous membrane with pore sizes ranging from 0.02 microns to about 0.6 microns. Alternatively, it can be a non-porous polymeric membrane which transports the active compound through dissolution in the polymer. Suitable polymers include ethylene vinyl-acetate, polyethylene, polypropylene, polyvinylchloride, cellulose acetate, cellulose nitrate, polyacrylonitrile, and polytetrafluoroethylene.

Detailed Description Text (10):

The diffusion rate limiting membrane 14 is the layer of the laminate that controls the rate at which the vapor or liquid is emitted or released from the active compound which is incorporated into the device. The release rate is a function of the thickness, the porosity, the tortuosity, the concentration gradient of the active compound across the membrane, and the diffusion coefficient of the compound. The active compound diffuses into the micropores of the diffusion rate limiting membrane layer and then is released at a substantially constant rate over the life of the device. This contrasts with the release mechanism of release devices lacking the rate limiting membrane which release very quickly early in their life and release at a significantly slowed rate thereafter.

Detailed Description Text (11):

Impermeable backing layer 16 is a material which does not allow the diffusion of gases and liquids. The backing provides a barrier to the diffusion of the active compound past the edge of the reservoir layer adjacent the impermeable backing layer.

Detailed Description Text (13):

For controlled release devices in which the reservoir layer 12 does not provide the

necessary "tacky" surface for adhering to the impermeable backing layer 16 and the diffusion rate limiting layer 14, it is desirable to provide a clip or other component for securing the layers of the device together. This component may be a miniature clip, such as the clip shown in phantom at 18 in FIG. 1 which is secured over each face of the device, or a small amount of an adhesive, such as an epoxy, applied to the edges. Alternatively, the laminate layer edges may be secured by heat or solvent sealing techniques. In addition to providing a support system for the layers of the device, the clip 18 or other components prevent the loss of the active component from the edges of the reservoir.

Detailed Description Text (14):

Active compounds which are contemplated within the scope of the present invention include vapor emitting compounds such as perfumes or other fragrances. More particularly, suitable vapor emitting compounds are naturally occurring essential oils, air fresheners, insecticides, and insect repellents. When the reservoir layer of the laminate incorporates one or more of a vapor emitting compound, the compound diffuses to the edge of the reservoir layer and comes into contact with the diffusion rate limiting membrane layer. The vapor emitting compound fills the pores as it diffuses and then is controllably vaporized at a substantially constant rate into the environment surrounding the device.

Detailed Description Text (15):

Additional active compounds also within the scope of the present invention are liquids or dissolved solids such as breath fresheners which are intended to be released into a liquid environment. When incorporated into the reservoir layer of the laminate with a diffusion rate control membrane layer, the liquid diffuses into the micropores of the membrane layer and then becomes solubilized by the liquid environment surrounding the device. When the active compound is a solid which is dissolved in a liquid the diffusions of the solid may be enhanced by prefilling the micropores with the appropriate liquid. In the case of a breath freshener this liquid is water.

Detailed Description Text (18):

FIG. 2 illustrates another embodiment of the present invention. FIG. 2 illustrates a laminate that consists of four layers: a reservoir layer 22, a diffusion rate limiting membrane layer 24, an impermeable backing layer 26, and a decorative layer 28. The reservoir layer 22, rate limiting membrane layer 24, and impermeable backing layer 26 have properties and characteristics as described for FIG. 1. Decorative layer 28 is preferably a thin permeable polymeric material which will readily transmit the active compound and at the same time provide an ornamental quality to the controlled release device. Useful applications of this decorative device include ornamental "jewelry" type pendants which incorporate a perfume or naturally occurring essential oil fragrance. This device will emit a perfume or fragrance for a period of from 6 hours to 24 hours. Such pendants can be worn for a day and then disposed of after a one time use. The decorative controlled release devices for emitting vapors used in this manner find a particularly advantageous utility by those persons who are allergic to perfumes or have otherwise incompatible skin types for wearing perfumes or fragrances.

Detailed Description Text (21):

FIG. 3 depicts another embodiment of the present invention, generally designated laminate 30. This preferred embodiment is suitable for adhering to a surface while emitting vapors, liquids, or dissolved solids of choice. In accordance with the teachings of the present invention the features of this embodiment include a diffusion rate limiting membrane 34, a reservoir layer 32, adjacent the diffusion rate limiting membrane layer, a vapor and liquid impermeable backing layer 36 adjacent the diffusion rate limiting membrane layer, and a pressure sensitive contact adhesive layer 38 adjacent the impermeable backing layer.

Detailed Description Text (22):

The diffusion rate limiting membrane 34 has the properties and characteristics as discussed above. The presence of the membrane is necessary for the effective control of the release rate of the active compound from the device. The membrane, as discussed above, is responsible for the substantially constant rate of release of the active compound over the life of the device.

Detailed Description Text (23):

Adjacent the diffusion rate limiting membrane layer 34 is the reservoir layer 32 incorporating the active compound of choice. Reservoir layer 32 may consist of any of the polymeric forms discussed above in the description of FIG. 1. Adjacent the reservoir layer 32 is a vapor and liquid impermeable backing 36. In addition to being a barrier to the active compound, the impermeable backing layer 36 further provides a means to prevent the active compound from interfering with the function of the adhesive as will be discussed below.

Detailed Description Text (24):

Adjacent the vapor and liquid impermeable backing 36 is an adhesive layer 38. The adhesive may be any pressure sensitive contact adhesive suitable for applying to a surface such as the acrylate contact adhesives. When the controlled release device is intended to be used on the skin or any tissue area of a person the contact adhesive must additionally be non-toxic, biocompatible, and hypoallergenic. In particular the biocompatible adhesive may be suitable acrylates, and hydroxypropyl cellulose, medical grade silicone adhesives and their derivatives.

Detailed Description Text (25):

The adhesive is applied to the impermeable backing layer 36 of the laminate. The backing material prevents the diffusing active compound from diffusing into the adhesive layer 38 and diminishing the effectiveness of the adhesive by solubilizing it or destroying the surface-adhesive bond. It is also undesirable for the active compound to diffuse in the direction of the adhesive since the target release point is the environment bound by the diffusion rate limiting membrane 34.

Detailed Description Text (29):

A variation of the embodiment of the present invention illustrated in FIG. 3 is detailed in the laminate of FIG. 4. In accordance with FIG. 4 a decorative layer 50 is adjacent the diffusion rate limiting membrane layer 44. A reservoir layer 42 is adjacent both the diffusion rate limiting, membrane layer 44, and an impermeable backing layer 46. An adhesive layer 48 is adjacent the impermeable backing layer 46. The diffusion rate limiting membrane 44, reservoir layer 42, impermeable backing layer 46, and adhesive layer 48 have properties and characteristics as described for FIG. 3. The decorative layer 50 preferably is comprised of a thin highly porous material of polyester base which freely allows the released vapors to diffuse from one surface to the other surface and into the surrounding environment.

Detailed Description Text (30):

A useful application of the laminate pictured in FIG. 4 is a perfume emitting device. The active compound is a vapor emitting perfume and is incorporated into the reservoir layer according to methods known in the art as described above. Further and in accordance with the present invention the perfume emitting device may be decoratively worn by adhering the device to the clothing or the skin of its user. By simply pressing the laminate to clothing or skin, the user has an attractive means to "wear" perfume. The diffusion rate limiting membrane used in combination with the reservoir layer which incorporates the perfume provides a means to effectively and continuously deliver a pleasing aroma at a substantially constant rate for a period of from 6 hours to 24 hours. Persons who prefer to wear perfume but are precluded from doing so because of allergies or skin chemistries are particularly suitable users for the perfume emitting device. Likewise, persons who are drawn to the long lasting scent of perfume on the body or the pleasing appearance of the decorative aspect or the variety afforded by the many different

designs which may be available are also potential users.

Detailed Description Text (34):

After the isopropyl alcohol was evaporated, a gas and liquid impermeable membrane layer consisting of an approximately 50 um membrane of a medium low density polyethylene/aluminized polyester/ethylene vinyl acetate was placed on the adhesive layer. A polymer gel of perfume emitting compound and hydroxypropyl cellulose was then prepared by adding enough of a perfume to powdered hydroxypropyl cellulose to prepare a 50% by weight perfume-polymer gel. The hydroxypropyl cellulose is KLUCEL with a molecular weight of 1,000,000.

Detailed Description Text (35):

The polymer-perfume gel was then spread onto the impermeable membrane layer forming the reservoir layer of the laminate. A diffusion rate limiting membrane consisting of a 40 um thick ethylene vinyl-acetate available from Bertak was then placed adjacent the reservoir layer.

Detailed Description Text (40):

A gas and liquid impermeable membrane layer consisting of an approximately 50 micron thick membrane layer of a medium low density polyethylene/aluminized polyester/ethylene vinyl acetate is placed on the adhesive layer. A polymer gel of insect repellent emitting compound and hydroxypropyl cellulose is then prepared by adding enough of an insect repellent to powdered hydroxypropyl cellulose to prepare a 50% by weight insect repellent-polymer gel. The hydroxypropyl cellulose is KLUCEL with a molecular weight of 1,000,000.

Detailed Description Text (41):

The polymer-insect repellent gel is then spread onto the impermeable membrane layer forming the reservoir layer of the laminate. A diffusion rate limiting membrane consisting of a 40 micron thick ethylene vinyl-acetate available from Bertak is then placed adjacent the reservoir layer.

Detailed Description Text (46):

A polymer gel comprising about 60% liquid flavoring material, e.g. mint, in a gelled gelatin is prepared by incorporating the mint in the gelatin-water system before it gels and allowing it to gel. The mint-gelatin gel is then spread onto the impermeable membrane layer forming the reservoir layer of the laminate and having a thickness of about 200 um. A diffusion rate limiting membrane consisting of a 50 to 100 um thick porous polytetrafluoroethylene film is then placed adjacent the reservoir layer. The resulting laminate is then cut into squares or circles of 1 to 2 cm.² for use as sustained release breath fresheners. The breath fresheners prepared in accordance with this invention may be adhered to tissue or tooth surfaces in the users mouth and will controllably release the mint at a constant rate over several hours.

Detailed Description Text (48):

A device useful for the sustained and controlled release of air fresheners comprising the general laminate form shown in FIG. 4 is prepared using the following procedure and materials. An acrylate adhesive is spread on a peeling layer of standard form release paper to a thickness of approximately 75 um. A gas and liquid impermeable membrane layer consisting of an approximately 200 um membrane of a medium low density polyethylene/aluminized polyester/ethylene vinyl acetate is placed on the adhesive layer. An air freshener is incorporated in a 400 um thick layer of ACCUREL porous polypropylene having a 80% void volume by immersing the ACCUREL in the air freshener for three hours. Following the immersion step the ACCUREL is placed on the impermeable membrane layer which is followed by placing a diffusion rate limiting membrane of cellulose nitrate having a pore size of about 0.1 microns. The device is finished with a decorative covering of polyester which provides an added ornamental appeal.

CLAIMS:

1. A device useful for the controlled release of a perfume or fragrance, said device forming a laminate comprising:

a decorative layer consisting of an artistic design formed on a 50 um polyester film;

a diffusion rate limiting membrane layer adjacent said decorative layer, said diffusion rate limiting membrane consisting of a 40 um thick ethylene vinyl-acetate film;

a reservoir layer adjacent said diffusion rate limiting membrane layer, said reservoir layer comprising a gelled mixture of perfume and hydroxypropyl cellulose;

a vapor and liquid impermeable backing layer adjacent said reservoir layer, said impermeable backing layer consisting of a 50 um thick medium density polyethylene/aluminized polyester/ethylene vinylacetate;

a pressure sensitive contact adhesive layer adjacent said vapor and liquid impermeable backing layer, said adhesive layer consisting of a medical grade silicone adhesive.